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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/925,635	08/09/2001	Nanna Kristensen Soni	4305/1H520US1	2913

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EXAMINER	
FOLEY, SHANON A	
ART UNIT	**PAPER NUMBER**
1648	

DATE MAILED: 03/23/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/925,635	SONI ET AL.	
	Examiner	Art Unit	
	Shanon Foley	1648	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *15 December 2003*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1,2,4-20,58,59,65 and 66* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1,2,4-16,18-20,58,59,65 and 66* is/are rejected.

7)☒ Claim(s) *17* is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☒ All b)☐ Some * c)☐ None of:

1.☒ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

In the paper submitted December 12, 2003, applicant cancelled claims 48-50, amended claims 1, 10, 14, 20 and added new claims 65 and 66. Claims 3, 21-47, 51-57 and 60-64 remain withdrawn from consideration due to a non-elected invention. Claims 1, 2, 4-20, 58, 59, 65 and 66 are under consideration.

It is noted that support for the second proviso in claim 65 is found on page 3, lines 14-16.

Election/Restrictions

This application contains claims 3, 21-47, 51-57 and 60-64 drawn to an invention nonelected with traverse in Paper No. 10. A complete reply to the final rejection must include cancelation of nonelected claims or other appropriate action (37 CFR 1.144) See MPEP § 821.01.

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 1, 2, 4-20, 58, 59 and 65 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

Claim 1 has been amended to state that the immunogenic substance is not DNA derived from cytomegalovirus. Applicant states on page 16 of the response that support for the

amendment is found on page 14, line 33 to page 15, line 18. However, upon review of the excerpt cited by applicant, it is determined that there is no support for the newly added negative proviso. Page 14, lines 18-20 recite:

> Examples of immunogenic substances are antigens, allergens, allergoids, peptides, proteins, haptens, carbohydrates, peptide nucleic acids (PNAS, a sort of synthetic genetic mimic), and viral or bacterial material...

Page 14, line 33 to page 15, line 18 provides examples of immunogenic substances encompassed by the invention:

> In particular such immunogenic substances may be...optionally inactivated or attenuated bacteria or virus as well as components thereof, RNA, **DNA**, PNA..., such derived from...**Cytomegalovirus**.... (emphasis added).

Therefore, there is *ipsis verbis* support in the disclosure recognizing cytomegalovirus DNA as an immunogenic substance. The specification does not teach, imply or suggest the newly added negative proviso. The courts have found that any negative limitation or exclusionary proviso must have basis in the original disclosure. See *Ex parte Grasselli*, 231 USPQ 393 (Bd. App. 1983), *aff'd mem.*, 738 F.2d 453 (Fed. Cir. 1984)

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (e) the invention was described in (1) an application for patent, published under section 122(b), by another filed in the United States before the invention by the applicant for patent or (2) a patent granted on an application for patent by another filed in the United States before the invention by the applicant for patent, except that an international application filed under the treaty defined in section 351(a) shall have the effects for purposes of this

subsection of an application filed in the United States only if the international application designated the United States and was published under Article 21(2) of such treaty in the English language.

Claims 1, 2, 4-8, 11-13, 16, 58, 59, and 66 are rejected under 35 U.S.C. 102(e) as being anticipated by Gonczol et al. (US 6,448,389).

Newly presented claim 66 is drawn to a parenteral vaccine comprising at least one immunogenic substance selected from and an adjuvant formed with a Group 2 element of the Period Table, i.e. magnesium hydroxide that is not combined with aluminum hydroxide or aluminum oxide and is not calcium hydroxide in gel combination with zinc hydroxide, lecithin and polyalphaolefine.

Gonczol et al. teach a vaccine formulation comprising DNA molecules expressing gB (an antigen) to induce immune responses to HCMV, see column 2, lines 22-27, column 4, line 63 to column 5, line 10. Gonczol et al. also teach suspending the DNA formulations in pharmaceutically acceptable carriers and incorporating a magnesium hydroxide adjuvant, see column 6, lines 31-41. Therefore, the teachings of Gonczol et al. anticipate claim 66.

In response to the rejection of claims 1, 2, 4-8, 11-13, 58 and 59, applicant notes that claim 1 has been amended to exclude DNA from cytomegalovirus antigens and is therefore different from the formulation of Gonczol et al. Applicant states on page 19 that although the specification discloses this source as a suitable immunogenic substance, the subject matter is no longer claimed.

Applicant's arguments and the amendment to the specification have been fully considered. However, as applicant has indicated, the specification discloses cytomegalovirus DNA as a suitable antigen. No support in the disclosure can be found for excluding this

particular virus or antigens derived from it. Therefore, the rejection of claims 1, 2, 4-8, 11-13, 58 and 59 is maintained for reasons of record.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

Claims 9, 10 and 20 are rejected under 35 U.S.C. 103(a) as being unpatentable over Gonczol et al. as applied to claims 1, 2, 4-8, 11-13, 16, 58, 59 and 66 above, and further in view of Vogel et al. ("A Compendium of Vaccine Adjuvants and Excipients" in Vaccine Design: The Subunit and Adjuvant Approach (Chapter 7), M.F. Powell & M.J. Newmann, Eds. (Plenum Press, New York) 1995, pp. 141-228), supplied by applicant in the IDS of paper no. 5 for reasons of record.

Applicant argues that Gonczol et al. do not teach the same formulation presently claimed and Vogel et al. do not render the invention obvious.

However, there is no support for the added proviso for excluding cytomegalovirus from the instant composition. Therefore, the rejection is maintained for reasons of record.

Claims 1, 2, 4-8, 11-13, 18, 58, 59 and 66 are rejected under 35 U.S.C. 103(a) as being unpatentable over Aviram et al. (US 6,362,236) and Conte et al. (US 5,464,633).

Claims 1, 2, 4-8, 11-13, 58 and 59 remain rejected for reasons of record. See the summary of claim 66 above.

Aviram et al. teach compositions and methods of administering a hydrolated cholesterol lowering agent, see claim 1 and examples 1-4 in columns 7-14. Aviram et al. teach that the hydrolated compounds are formulated for parenteral administration, as well as common excipients and carriers, such as titanium dioxide, see column 14, lines 8-13.

Although Aviram et al. do not teach that titanium dioxide is an adjuvant, Conte et al. specifically identifies titanium dioxide as an adjuvant by stating that "titanium dioxide and other adjuvants well known to the skilled in the field, may be used", see column 6, lines 17-18. Therefore, the adjuvanting property of titanium dioxide is well known in the art.

Neither reference teaches combining or administering titanium dioxide in a vaccine formulation. However, it is notoriously conventional in the vaccine art to administer art-recognized adjuvants in vaccine formulations to boost an immune response against a target antigen. Therefore, combining the art-recognized adjuvant, titanium oxide, in a vaccine formulation would have been prima facie obvious to one of ordinary skill in the art at the time the invention was made with a reasonable expectation of success, absent evidence to the contrary.

Applicant argues that Avarim et al. do not teach an immunogen and that the molecular weight of the cholesterol-lowering agent is lower than that of the instant immunogen. Applicant further states that Conte et al. do not teach titanium dioxide is an adjuvant, but is an opacity agent. Applicant also argues that the subject matter of Conte et al. is not related to the field of parenteral vaccines. Applicant asserts that there is no evidence that titanium dioxide has adjuvant properties and the ordinary artisan would have no motivation or reasonable expectation of success for using it in a vaccine composition.

Applicant's arguments have been fully considered, but are found unpersuasive. It is conceded that Avarim et al. do not teach an immunogen. However, the reference combines an agent that treats with titanium dioxide, see the previous citations. Avarim et al. do not teach that titanium dioxide is an adjuvant. However, it is clear from the teachings of Conte et al. that titanium dioxide is an adjuvant. In the passage on column 6, Conte et al. list plasticizing substances with "different molecular weight and opacity agents as titanium dioxide and other adjuvants well known to the skilled in the field...". It appears from the teachings of Conte et al. that titanium dioxide is an opacity agent, but that opacity agents are adjuvants because of the phrase, "and other adjuvants" after recitation of "titanium dioxide". The reference lists a specific example followed by, "and other adjuvants" to clearly designate what the nature of the specific example, titanium dioxide, is. Therefore, it is clear that titanium dioxide has adjuvant properties and the ordinary artisan would have a reasonable expectation of success for using it in a vaccine composition.

Regarding the field of Conte et al., pharmaceutical tablets releasing an active substance is directly related to administering an immunogen or antigen in a vaccine formulation. Obviousness can only be established by combining or modifying the teachings of the prior art to produce the claimed invention where there is some teaching, suggestion, or motivation to do so found either in the references themselves or in the knowledge generally available to one of ordinary skill in the art (emphasis added). See *In re Fine*, 837 F.2d 1071, 5 USPQ2d 1596 (Fed. Cir. 1988) and *In re Jones*, 958 F.2d 347, 21 USPQ2d 1941 (Fed. Cir. 1992). It is notoriously conventional in the vaccine art to administer immunogens with art-recognized adjuvants in vaccine formulations to boost an immune response against an immunogen. Avarim et al. and

Conte et al. teach combining and administering titanium dioxide with active agents. An example of active agents disclosed by Conte et al. are biological peptides such as insulin, see claim 7 for example. It would have been prima facie obvious to one of ordinary skill in the art at the time the invention was made to combine other biological peptides, such as an immunogen with an art-recognized adjuvant, such as titanium dioxide with a reasonable expectation of success, absent evidence to the contrary.

Claims 14, 15 and 65 are rejected under 35 U.S.C. 103(a) as being unpatentable over Gonczol et al. as applied to claims 1, 2, 4-8, 11-13, 16, 58, 59 and 66, or alternatively Aviram et al. and Conte et al. as applied to claims 1, 2, 4-8, 11-13, 18, 58, 59 and 66 above.

Claim 65 states that the adjuvant is present in an amount from about 0.004 to about 12M.

See the teachings of Gonczol et al. or Aviram et al. and Conte et al. previously discussed in the prior Office action. None of the references teach the concentration of the cation recited in the claims. However, each set of references teach using the claimed salts in compositions that are parenterally administered, which would necessarily comprise a molar concentration of cation within each composition. In addition, it is conventional practice in the vaccine arts to optimize the amount of components within a composition for individual administrations. Therefore, each concentration within the recited molar range of cations would have been prima facie obvious alternatives to one another to one of ordinary skill in the art at the time the invention was made, absent unexpected results to the contrary.

Applicant did not specifically address the rejection of claims 14 and 15 in the response. It is presumed that this is an inadvertent omission. The rejection of these claims is maintained for reasons of record.

Claim 19 is rejected under 35 U.S.C. 103(a) as being unpatentable over Gonczol et al. as applied to claims 1, 2, 4-8, 11-13, 16, 58, 59 and 66 above, and further in view of Aviram et al. and Conte et al. for reasons of record.

Applicant argues that Gonczol et al. do not teach the instant formulation and that adding the teachings of Aviram et al. and Conte et al. does not render the invention obvious.

Applicant's arguments have been fully considered, but are found unpersuasive. There is no support in the disclosure for excluding DNA from cytomegalovirus. Further, Conte et al. identifies titanium dioxide as an adjuvant. Therefore, the rejection is maintained for reasons of record.

Allowable Subject Matter

Although the previous action erroneously indicated that claim 17 was allowable, the claim should have been objected to as being dependent upon a rejected claim. The examiner apologizes for any inconvenience. The claim remains drawn to allowable subject matter for reasons set forth previously.

Claim 17 is objected to as being dependent upon a rejected base claim, but would be allowable if rewritten in independent form including all of the limitations of the base claim and any intervening claims.

Conclusion

Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Shanon Foley whose telephone number is (571) 272-0898. The examiner can normally be reached on M-F 9:30 AM - 6:00 PM.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, James Housel can be reached on (571) 272-0902. The fax phone number for the organization where this application or proceeding is assigned is 703-872-9306.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Shanon Foley

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